REMARKS

Claims 1-4, 12, 15, 17-22, 24, 27, and 29-32 are pending. Claims 1, 2, and 18 have been amended and new claims 30-32 have been added. Claims 11, 16, 23, 25, and 26 have been withdrawn from further consideration. Claims 5-10, 13, 14, and 28 have been canceled.

Support for the amendments to claim 1 may be found, *inter alia*, on page 18, line 26 to page 19, line 5. Support for new claims 30 and 31 may be found, *inter alia*, on page 16, lines 7-12. Support for new claim 32 may be found, *inter alia*, on page 16, line 16 to page 19, line 5. Support for new claim 33 may be found, *inter alia*, in claim 28. Support for new claim 34 may be found, *inter alia*, on page 7, line 26 to page 8, line 10.

Applicants acknowledge the withdrawal of all of the rejections under 35 U.S.C. § 112, second paragraph made in the Office Action mailed October 1, 2007.

I. *The rejections under 35 U.S.C. § 103(a) should be withdrawn*

Claims 1-4, 8, 11, 15, 17, 18, and 27-29 stand rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 5,980,882 to Eichman (hereinafter "Eichman") for the reasons set forth on pages 4 and 5 of the Office Action. Claims 1-4, 8, 11, 12, 15, 17, 18, 21, 22, 24, and 27-29 stand rejected under 35 U.S.C. § 103(a) over Eichman in view of U.S. Patent No. 6,699,506 to Paillard *et al.* (hereinafter "Paillard") for the reasons set forth on pages 5 and 6 of the Office Action. Finally, claims 19 and 20 stand rejected under 35 U.S.C. § 103(a) over Eichman and Paillard in view of U.S. Patent No. 6,602,911 to Kranzler *et al.* (hereinafter "Kranzler").

The present invention relates to a multiparticulate milnacipran composition for oral administration comprising particles comprising a milnacipran salt complexed with an ion-exchange resin, wherein:

(a) the particles lack an impregnating agent; and

(b) the particles are coated with an enteric polymer.

The composition provides delayed and extended release of milnacipran and produces a therapeutic effect over approximately 24 hours when administered to a patient in need thereof, with diminished incidence or reduced intensity of side effects relative to the side effects resulting from administration of the same dose of milnacipran administered in an immediate release formulation.

As set forth in greater detail below, far from providing one of ordinary skill in the art with a reason to prepare a formulation as claimed, the prior art actually teaches away from the invention by disclosing that an impregnating agent, which the present invention expressly excludes, is a necessary component thereof.

More particularly, at the time the invention was made, one of ordinary skill in the art would not have expected to obtain a coated ion-exchange resin particle that did not peel or crack when exposed to water or biological fluids unless he/she used an impregnating agent (also known as a solvating agent) during complexation or after complexation of the drug with the resin. Such cracking and peeling would lead to the complete undermining of the extended and/or delayed release characteristics of any coated dosage form.

For example, in U.S. Patent No. 4,221,778 to Raghunathan discloses that:

> "[i]initial attempts to retard . . . rapid release of drug by the use of diffusion barrier coating were relatively ineffective . . . since the coating tended to peel rapidly and the coated particles swelled and tended to fracture when contacted by water or biological fluids. It has now been discovered that the tendency of ion exchange resin drug complex particles to swell and fracture in biological fluids can be overcome by the use of solvating agents such as polyethylene glycol."

Raghunathan at column 2, lines 36-45.

The only way that the skilled artisan could hope to get away from using an impregnating agent, and still obtain a coated resin particle that did not peel or crack when exposed to water or biological fluids, was to use the free base of a drug, not the salt form of the drug. *See, e.g.*, U.S. Patent No. 4,996,047 to Kelleher and U.S. Patent No. 4,894,239 to Nomura. Accordingly, the art teaches away from the claimed invention. Contrary the teachings of the art, the claimed multiparticulate milnacipran composition for oral administration comprising particles comprising milnacipran complexed with an ion-exchange resin unexpectedly has a stable enteric coating, even though an impregnating agent is not present and even though the salt form of the drug is used. For at least this reason, Eichman does not render claim 1, from which all of the pending claims ultimately depend, obvious. Also, Eichman even in view of Paillard and Kranzler, do not render the claims obvious because neither Paillard nor Kranzler remedies the deficiencies in Eichman. Reconsideration and withdrawal of the rejection of claims are respectfully requested.

Eichman discloses a pharmaceutical composition comprising a drug-resin complex and a chelating agent in which the composition is in the form of a solid or a gel. In Example 1 of Eichman, he uses an impregnating agent, specifically polyethylene glycol, during the complexation step between the resin and the drug. Accordingly, Eichman appears to teach away form multiparticulate milnacipran compositions for oral administration comprising particles comprising a milnacipran salt complexed with an ion-exchange resin, wherein the particles lack an impregnating agent, as presently claimed.

The deficiencies in Eichman are not cured by Paillard and/or Kranzler. Paillard teaches a pharmaceutical composition with prolonged release, for oral administration of a single daily dose of milnacipran, having a multi-particulate form containing a plurality of microgranules each comprising an active microsphere containing a saccharose and/or starch nucleus and a binding agent, each microgranule being coated with a film having a base of at least one polymer insoluble in water, but permeable to physiological liquids. As an initial matter, it is clear that Paillard does not even use ion exchange resins in his compositions. Also, Paillard, even in view of Eichman, does not teach multiparticulate milnacipran compositions for oral administration comprising particles comprising a milnacipran salt complexed with an ion-exchange resin, wherein the particles lack an impregnating agent.

Kranzler discloses a method of treating fibromyalgia syndrome (FMS), chronic fatigue syndrome (CFS), and pain in an animal subject involving administering a therapeutically effective amount of a dual serotonin norepinephrine reuptake inhibitor compound or a pharmaceutically acceptable salt thereof, wherein the dual serotonin norepinephrine reuptake inhibitor compound has a non-tricyclic structure and an equal or greater inhibition of norepinephrine reuptake than serotonin reuptake. In particular, the use of milnacipran to treat FMS, CFS, and pain is disclosed. Although Kranzler discloses the use of ion exchange resins for the delivery of such inhibitors, it does so in the context of a depot preparation. In other words, even in view of Eichman and Paillard, Kranzler does not disclose multiparticulate milnacipran compositions for **oral** administration comprising particles comprising a milnacipran salt complexed with an ion-exchange resin, wherein the particles lack an impregnating agent. And, the Examiner has not provided any evidence as to why the skilled artisan would have expected to orally administer Kranzler's composition, which is a depot preparation, to successfully treat FMS, CFS, and pain.

II. *The double patenting rejections should be held in abeyance*

Claim 28 stands rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claim 27 of co-pending Application No. 11/192,697 in view of Eichman and Paillard. Claims 1, 8, 13, 15, 20, 21, 22, and 24 also stand rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 12, and 16-18 of co-pending Application No. 10/690,872 in view of Eichman and Paillard. Claim 27 also stands rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claim 24 of co-pending Application No. 10/690,947 in view of Eichman and Paillard. Claims 1, 8, 15, 17, 18, and 20-22 also stand rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 9, 12, and 15-17 of co-pending Application No. 10/691,936 in view of Eichman and Paillard. Finally, claims 1, 8, 10, 15, 20, 21, and 24 also stand rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 11, 14-16, 18, and 19 of co-pending Application No. 11/192,885 in view of Eichman and Paillard.

Applicants submit that all of the foregoing rejections under the judicially created doctrine of obviousness-type double patenting may be overcome by filing of a terminal disclaimer.

Applicants acknowledge the provisional rejection of the aforementioned claims over the claims of the aforementioned co-pending applications in combination with Eichman and Paillard under non-statutory-type double patenting. Applicants also understand that the Examiner will continue to make this rejection as long as there are allegedly conflicting claims in each application, until the double patenting rejections are the only rejections remaining in at least one of the aforementioned applications. Applicants are prepared to file a suitable terminal disclaimer once claims have been agreed to be otherwise allowable.

Applicant respectfully submits that the pending claims are in condition for allowance.

Respectfully submitted,
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Dated: July 1, 2008

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